in international public health. This is achieved through: specialized surveillance networks; outbreak verification.

The World Health Organization (WHO) recognizes the importance of its partners in global epidemic surveillance and seeks to identify more effective ways of working with collaborating institutions. To this end the WHO global epidemic surveillance team links with a number of international networks for specific disease threats.

To investigate and follow up outbreak reports, an innovative mechanism - outbreak verification - was established at WHO headquarters in early 1997. Its aim is to improve epidemic disease control by actively collecting and verifying information on reported outbreaks and informing key public health professionals of confirmed and unconfirmed outbreaks which are potentially of international public health importance. Outbreaks are assessed for their importance to international public health (an outbreak with potential for international spread, a need for international response, or a potential impact on international travel or trade). Active follow-up with affected countries is undertaken to verify the existence of the epidemic, its cause and the response being put in place. WHO offers assistance in all cases.

S25 - Pathogenicity islands and other horizontal . . .

WeS11 How do we protect ourselves against an outbreak of hemorrhagic fever

A. Vaheri
Department of Virology, Haartman Institute, University of Helsinki, Finland

Viral hemorrhagic fevers (VHFs) are caused by arenaviruses (Lassa fever, South American HFs), filoviruses (Ebola, Marburg), bunyaviruses (Crimean-Congo HF, HFRS, Rift Valley fever) and flaviviruses (dengue HF, yellow fever). VHFs are zoonoses, prime examples of emerging infectious diseases, several with dramatic clinical course and high mortality. Only CGHF and hantaviral HFRSs have known animal reservoirs in Europe but VHFs may be acquired abroad or, very rarely, in a laboratory setting, or from an imported animal. The dramatic nature of VHF outbreaks easily generates excessive media attention. Some VHFs are considered potential weapons of bioterrorism. Thus there is increasing awareness to develop better means to manage and control VHFs. Much can be done. (i) National guidelines. Here we should remember that person-to-person spread of VHFs requires direct contact (blood, excreta) and that ribavirin is effective against several VHFs. (ii) Effective channels of communication. Internet services currently include WHO Outbreak Verification List, ProMed, and Euro-Surveillance; specialized net on-line journals such as "Emerging Infectious Diseases" are also useful. (iii) Increased preparedness for rapid diagnostics and international outbreak response (task force). In the multinational Europe, unlike at CDC in the US, the diagnostic facilities are still limited. While both rapid and safe tests (PCR, strip tests) as well as reliable reference tests and BSL-4 laboratories are needed, the first thing to suspect is still malaria. The "European Network for Diagnostics of Imported Viral Diseases" has built a network of European laboratories working on diagnostics of imported, rare, and emerging viral infections.

WeS13 Pathogenicity islands of gram-negative bacteria: Functional and evolutionary aspects

J. Heesemann
Max von Pettenkofer-Institut, Munich, Germany

In the early years of Medical Microbiology pathogenic bacteria were characterized phenotypically by one virulence factor (e.g. toxin). Later, the high complexity and variability of pathogenic bacteria became evident. In analogy to evolution of antibiotic resistance, transposons, plasmids, phages and large mobile chromosomally integrated units (phathogenicity islands, PAI) have been identified as carriers of pathogenicity genes and virulons. Human pathogenic and opportunistic Gram-negative bacteria are frequently carriers of PAIs. A complete PAI is flanked by short directed repeats and carries genes for PAI mobility (e.g. integrase). Many PAIs consist of several modules which encode for type III secretion systems, several antihost effector proteins, adhesins, ferric iron uptake systems and carry DNA regions of phage or plasmid origin. Because of their mobility PAIs can disseminate into diverse species and thus generate new pathotypes. For Escherichia coli more than six PAIs have been identified. The PAI-pattern determines the pathotype of E. coli e.g. EHEC, EPEC, UTEC. Interestingly, the majority of strains isolated from blood culture or urine of patients carry the PAI of Yersinia pestis (denoted as HPI). In Salmonella enterica SPI-1 is involved in intestinal invasion and SPI-2 in intracellular survival. The impact of PaIs in evolution of Samonella, Yersinia and Escherichia coli will be discussed.

WeS14 Bacterial crosstalk: Interaction between Yersinia and its target cell

H. Wolf-Watz
Cell and Molecular Biology, Umeå, Sweden University

We are using *Yersinia pseudotuberculosis* as a model to understand the basic mechanisms behind the cell-contact dependent induction and subsequent polarized translocation of the effector proteins (Yops) into the cytosol of the target cell. *Y. pseudotuberculosis* up-regulates Yop-expression after an intimate contact between the pathogen and its target cell has been established. This cross-talk involves also the Type III secretion machine. The translocation mechanism is polarized and is dependent on at least three proteins YopB, YopD and LcrV respectively. Our results suggest that the YopB, YopD and LcrV are involved in forming a pore in the membrane of the target cell. After translocation, the different Yop-effectors are targeted to different regions of the eukaryotic cell. The protein-tyrosine phosphatase YopH, showing high homology with eukaryotic PTPases, blocks immediate early phosphorylation signals after infection. YopH is targeted to focaladhesions leading to disruption of these structures. YopE works in concert with YopH and these two proteins are essential for the pathogen to block phagocytosis. YopE possesses a GAP activity which inactivates proteins of the Rho-family of small G-proteins leading to disruption of cell's cytoskeleton.

WeS15 Comparative and functional genomics of Neisseria

X. Nassif
INSERM U411, Faculté Necker-Enfants Malades, Paris, France

Neisseria meningitidis (Nm), *Neisseria gonorrhoeae* (Ng), and *Neisseria lactamica* (Nl) belong to the same genospecies. However, they express dramatically different pathogenesis. Nm colonizes the nasopharynx and is responsible for septicemia and meningitis, Ng gives rise to a localised infection, and Nl has never been associated to a disease and is therefore believed to be non pathogenic. Considering that both Nm and Ng are human pathogens which do not survive in the environment and which colonize and invade mucosa at their port of entry, it is likely that they share common characteristics which are not found in the non pathogenic Nl. Furthermore N. meningitidis may express specific virulence factors responsible for the bloodstream dissemination and the crossing of the blood brain barrier. These properties of pathogenic Neisseria may be determined by specific chromosomal regions. To address this issue, we used a combination of both subtractive hybridization and hybridization of DNA arrays to identify chromosomal regions specific for Nm and common between Nm and N.g. These experiments confirmed that Nm has specific chromosomal regions and others which are shared with Ng. An analysis of the content of these regions as well as the consequences of the mutagenesis of some of these regions will be presented and tested in several models believed to be associated with virulence.

S26 - *In vitro veritas?* Clinical implications of . . .

WeS20 How to report susceptibility results to clinicians

R. Auckenthaler
University HospitalSwitzerland

Susceptibility test determine the susceptibility of bacteria against antibiotics. They are necessary to detect acquired resistance. For the clinician the development of resistance makes the adequate prescription of antibiotics more difficult Historically susceptibility tests have been performed by disk diffusion. Today they include disk diffusion, growth of bacteria at various antibiotic concentration or direct determination of MIC. All methods correlate presumed or calculated MIC to the in vivo activity, reporting sensitive, intermediate or resistant strains predicting the likely probability of clinical success. Susceptibility tests allow to 1) the adapted prescription of antimicrobial agents for a precise pathogen, 2) to follow epidemiological trends of resistance, useful for empirical therapy, 3) detection of multi-resistant strains with risk of nosocomial dissemination.